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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,929	10/18/2001	Janet Newman	10342-0010-999	4507

24341 7590 01/02/2004

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EXAMINER	
HO, ALLEN C	

ART UNIT	PAPER NUMBER
2882	

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,929	NEWMAN ET AL.	
	Examiner	Art Unit	
	Allen C. Ho	2882	

-- The MAILING DATE of this communication appears on the cover sheet with th correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 8-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 8-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0803,1103*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Drawings

1. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the a charged-coupled device (CCD) camera and a phosphor plate imaging system as claimed by claims 5, 6, 46, and 47 must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

2. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the CCD camera comprising a phosphor screen as claimed in claims 32 and 37 must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

3. Claim 14 objected to because of the following informalities: line 3, "another" should be replaced by --other--. Appropriate correction is required.

4. Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 15 recites determining the presence of the crystalline material in the *in-situ* growth environment prior to irradiating, which is similar to the first method step recited by claim 11.

5. Claim19 is objected to because it is identical to claim 14.

6. Claim 34 is objected to because of the following informalities:

(1) Line 8, "growing incubator" should be replaced by --growth environments--. See claim 1.

(2) The last paragraph should be deleted (see claim 1).

Appropriate correction is required.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1, 3, 4, 8, 9, 11-21, 25-28, 34, 35, 39-45, 48, 49, and 51 are rejected under 35 U.S.C. 102(e) as being anticipated by Lehmann (U. S. Patent No. 6,507,636 B1).

With regard to claim 1, Lehmann disclosed an apparatus for detecting the presence of crystalline material in its *in-situ* growth environment, comprising: a crystal growing incubator (**1-4**) having opposing first (top) and second (bottom) sides and multiple crystal growth environments (**4**); an x-ray system, comprising: an x-ray source (column 5, line 26-27) disposed adjacent to the first side of the crystal growing incubator, where the x-ray source is configured to

irradiate crystalline material grown in the crystal growth environments; an x-ray detector (column 5, lines 34-37) disposed adjacent to the second side (in transmission geometry, column 2, lines 31-37) configured to detect the presence of diffracted x-rays from crystalline material grown in the crystal growing incubator; and a positioner (column 5, lines 29-30) that positions the x-ray system and each of the crystal growth environments relative to one another.

With regard to claim 3, Lehmann disclosed the apparatus of claim 1, wherein the crystal-growing incubator is a sample-holding tray that is configured to grow crystals therein.

With regard to claim 4, Lehmann disclosed the apparatus of claim 1, further comprising an imaging system (video microscope, column 5, lines 38-40) disposed adjacent to the crystal-growing incubator.

With regard to claim 8, Lehmann disclosed the apparatus of claim 1, wherein the x-ray source emits a monochromatic beam of x-rays consisting of CuKα radiation (column 5, line 41).

With regard to claim 9, Lehmann disclosed the apparatus of claim 1, wherein the x-ray source emits an x-ray beam with a focus size of 200 μm or less (column 5, lines 27-29).

With regard to claim 43, Lehmann disclosed the apparatus of claim 1, wherein the multiple crystal growth environments form an array.

With regard to claims 11, 15, and 20, Lehmann disclosed a method (column 2, lines 48-54) of screening crystalline material in its *in-situ* growth environment, the method comprising the steps of: identifying crystalline material in at least one of multiple *in-situ* growth environment (by optical microscopy); for each *in-situ* growth environment identified as having a crystalline material: aligning the crystalline material and an x-ray system with one another (column 5, lines 29-30); irradiating the crystalline material in the *in-situ* growth environment

with an x-ray beam from the x-ray system; and detecting a diffraction pattern from the crystalline material.

With regard to claim 12, Lehmann disclosed the method of claim 11, wherein the crystalline material is comprised of a group consisting of: a crystalline powder, a micro-crystal, a single crystal, an a plurality of single crystals (column 2, line 22).

With regard to claim 13, Lehmann disclosed the method of claim 11, wherein the diffraction pattern is comprised of a group consisting of: a powder diffraction pattern (produced by polycrystalline samples) and a pattern of x-ray diffraction spots (produced by single crystals).

With regard to claims 14 and 19, Lehmann disclosed the method of claim 11, further comprising, prior to irradiating, positioning (column 5, lines 29-30) the crystalline material and the x-ray beam relative to one another (inherent).

With regard to claim 16, Lehmann disclosed the method of claim 15, further comprising ascertaining the location of the crystalline material in the *in-situ* growth environment (This is inherent for aligning the crystalline material and the x-ray system.

With regard to claims 17 and 18, Lehmann disclosed the method of claim 16, further comprising storing the location of the crystalline material (This is inherent. The motorized programmable sample translation stage must be programmed with the location of the crystalline material).

With regard to claim 21, Lehmann disclosed a method of claim 11, wherein the growing further comprises producing crystalline material in the growth environment by a method selected from a group consisting of: a vapor diffusion method, a hanging-drop method, a sitting drop

method, a dialysis method, a microbatch method, and a gel crystal growth method (column 2, lines 26-30).

With regard to claim 25, Lehmann disclosed a method (column 2, lines 48-54) of screening for crystalline material in its *in-situ* growth environment, the method comprising the steps of: growing crystalline material in a crystal growing incubator (**1-4**) having multiple crystal growth environments (**4**); placing the crystal growth incubator into a positioner (column 5, lines 29-30); determining the presence of the crystalline material in at least one of the crystal growth environments (by optical microscopy); ascertaining the location of the crystalline material in the at least one of the crystal growth environments; storing the location of the crystalline material (This is inherent. The motorized programmable sample translation stage must be programmed with the location of the crystalline material); for each crystal growth environment identified as having crystalline material: positioning (column 5, lines 29-30) the crystal growing incubator and an x-ray source relative to each other based on the location of the crystalline material, such that an x-ray beam emitted from the x-ray source accurately aligns with the crystalline material; irradiating the crystalline material with the x-ray beam; detecting with an x-ray detector a diffraction pattern from the crystalline material; and detecting the diffraction pattern generated from the irradiating.

With regard to claim 26, Lehmann disclosed the method of claim 25, wherein the crystalline material is comprised of a group consisting of: a crystalline powder, a microcrystal, a single crystal, and a plurality of single crystals (column 2, line 22).

With regard to claim 27, Lehmann disclosed the method of claim 25, wherein the diffraction pattern is comprised of a group consisting of: a powder diffraction pattern (produced by polycrystalline samples) and a pattern of x-ray diffraction spots (produced by single crystals).

With regard to claim 28, Lehmann disclosed the method of claim 25, wherein the crystalline material is re-positioned relative to the x-ray beam while the x-ray beam remains stationary (sample translation stage).

With regard to claim 34, Lehmann disclosed an apparatus for detecting the presence of crystalline material in its *in-situ* growth environment, comprising: a crystal growing incubator (**1-4**) having opposing first (top) and second (bottom) sides, where the crystal growing incubator includes an array of crystal growth environments (**4**); an x-ray system, comprising: an x-ray source (column 5, line 26-27) disposed adjacent to the first side of the crystal growing incubator, where the x-ray source is configured to irradiate crystalline material grown in the crystal growth environments; an x-ray detector (column 5, lines 34-37) disposed adjacent to the second side (in transmission geometry, column 2, lines 31-37) configured to detect the presence of diffracted x-rays from crystalline material grown in the crystal growing incubator; and a positioner (column 5, lines 29-30) configured to sequentially align each of the crystal growth environments and the x-ray system with one another (column 4, lines 47-48).

With regard to claim 35, Lehmann disclosed the apparatus of claim 34, further comprising an imaging system (video microscope, column 5, lines 38-40) disposed adjacent to the crystal-growing incubator.

With regard to claim 44, Lehmann disclosed an apparatus for detecting the presence of crystalline material in it *in-situ* growth environment, comprising: an crystal growing

incubator (**1-4**) having opposing first (top) and second (bottom) sides and multiple crystal growth environments (**4**); an x-ray system, comprising: an x-ray source (column 5, line 26-27) disposed adjacent to the first side of the crystal growing incubator, where the x-ray source is configured to irradiate crystalline material grown in the crystal growth environments; an x-ray detector (column 5, lines 34-37) disposed adjacent to the second side (in transmission geometry, column 2, lines 31-37) configured to detect the presence of diffracted x-rays from crystalline material grown in the crystal growing incubator; an imaging system (video microscope, column 5, lines 38-40) disposed adjacent to the crystal-growing incubator, wherein the imaging system is configured to detect (by optical microscopy) the presence and location of crystals grown in the multiple crystal growth environments; and a positioner (column 5, lines 29-30) configured to sequentially align each of the crystal growth environments and the x-ray system with one another (column 4, lines 47-48).

With regard to claim 45, Lehmann disclosed the apparatus of claim 44, wherein the crystal-growing incubator is a sample-holding tray that is configured to grow crystals therein.

With regard to claim 48, Lehmann disclosed the apparatus of claim 44, wherein the x-ray source emits a monochromatic beam of x-rays consisting of CuKα radiation (column 5, line 41).

With regard to claim 49, Lehmann disclosed the apparatus of claim 44, wherein the x-ray source emits an x-ray beam with a focus size of 200 μm or less (column 5, lines 27-29).

With regard to claim 51, Lehmann disclosed the apparatus of claim 44, wherein the crystalline material is comprised of a group consisting of: a crystalline powder, a microcrystal, a single crystal, an a plurality of single crystals (column 2, line 22).

With regard to claims 39-42, these claims recite the type of crystalline materials being grown in crystal growth environments of the claimed apparatus. As such these claims are directed to intended use of the claimed apparatus and do not distinguish over the prior art. Accordingly, these claims are rejected for the reason set forth above. See MPEP §§ 2114 and 2115.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 5, 6, 32, 33, 36, 37, 38, 46, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lehmann (U. S. Patent No. 6,507,636 B1) as applied to claims 1, 34, and 44 above, and further in view of Stettner *et al.* (U. S. Patent No. 5,629,524).

With regard to claims 5, 6, 36, 46, and 47, Lehmann disclosed the apparatus of claims 1, 34, and 44. However, Lehmann failed to teach that the x-ray detector is a phosphor plate imaging system.

Stettner *et al.* disclosed that phosphor plate imaging systems are used with x-ray crystallographic analysis. Stettner *et al.* taught that phosphor plates have much greater dynamic range than film and are much more convenient to use because a laser readout leads directly to a digitized image (column 1, lines 24-27).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a phosphor plate imaging system for detecting diffracted x-rays, since a person would be motivated to obtain a digitized image for analysis.

With regard to claims 32 and 37, Lehmann disclosed the apparatus of claims 1 and 34. However, Lehmann failed to teach that the x-ray detector comprises a CCD camera comprising a phosphor screen.

Stettner *et al.* disclosed an x-ray detector that comprises a CCD camera comprising a phosphor screen (column 1, lines 45-60). Stettner *et al.* taught that an area larger than the CCD can be used to collect x-rays by using a fiber-optic coupler.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a CCD camera comprising a phosphor screen, since a person would be motivated to collect x-rays from a large area, which is greater than the detecting area of a CCD.

With regard to claims 33 and 38, Lehmann disclosed the apparatus of claims 32 and 37. However, Lehmann failed to teach that the phosphor screen achieves at least 4 to 8 line-pairs per mm resolution.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a phosphor screen with at least 4 to 8 line-pairs per mm resolution, since a person would be motivated to measure an x-ray diffraction pattern with sufficient resolution to separate the diffraction spots.

11. Claims 10 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lehmann (U. S. Patent No. 6,507,636 B1) as applied to claims 1 and 44 above, and further in view of Polichar *et al.* (U. S. Patent No. 6,205,199 B1).

With regard to claims 10 and 50, Lehmann disclosed the apparatus of claims 1 and 44. However, Lehmann failed to teach that the apparatus further comprises a transmitter that transmits information associated with the diffraction pattern to a remote location.

Polichar *et al.* disclosed an x-ray system that comprises a transmitter (modem, Ethernet) for transmitting data to remote locations for evaluation by experts who are not on site.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to provide a transmitter for transmitting data to remote locations, since a person would be motivated to consult with experts at remote locations.

12. Claims 22 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lehmann (U. S. Patent No. 6,507,636 B1) as applied to claims 11 and 25 above, and further in view of Arnowitz *et al.* (U. S. Patent No. 6,468,346 B2).

With regard to claims 22 and 29, Lehmann disclosed the method of claims 11 and 25. However, Lehmann failed to teach that the method is performed in space.

Arnowitz *et al.* disclosed that space-grown crystals are of higher crystallographic perfection than earth-grown crystals (column 2, lines 14-17).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to perform this method in space, since a person would be motivated to grow crystals with fewer defects that are suitable for use in either practical applications or crystallography.

13. Claims 23, 24, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lehmann (U. S. Patent No. 6,507,636 B1) as applied to claims 11 and 25 above.

With regard to claims 23, 24, 30, and 31, Lehmann disclosed the method the method of claims 11 and 25. However, Lehmann failed to teach determining whether the crystalline material is a protein crystal or a salt crystal.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine whether the crystalline material is a protein crystal or a salt crystal, since a person in the art would be able to make that determination given the x-ray diffraction pattern.

Response to Arguments

14. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

(1) Hajduk *et al.* (U. S. Patent No. 6,605,473 B1) disclosed a method for characterizing libraries of different materials using x-ray scattering.

(2) Durst *et al.* (U. S. Pub. No. 2003/0147496 A1) disclosed a diffraction system for biological crystal screening.

(3) Koinuma *et al.* (U. S. Patent No. 6,459,763 B1) disclosed a combinatorial x-ray diffractometer.

(4) Olson *et al.* (U. S. Patent No. 6,404,849 B1) disclosed an automated sample handler for x-ray crystallography.

(5) Carter (U. S. Patent No. 5,419,278) disclosed a vapor equilibrium tray for growing protein crystals.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allen C. Ho whose telephone number is (703) 308-6189. The examiner can normally be reached on Monday - Friday from 8:00 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Edward J. Glick can be reached at (703) 308-4858. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9318.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0530.

Allen C. Ho
Patent Examiner
Art Unit 2882

ACH ACH 12.11.03

EDWARD J. GLICK
SUPERVISORY PATENT EXAMINER